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## **COVID-19 and Parkinson's disease: what we know so far?**

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## **ABSTRACT**

### **Background**

Neurological diseases could negatively affect the outcome of Coronavirus-disease-2019 (COVID-19). However, the impact of COVID-19 in patients with neurodegenerative diseases, including Parkinson's disease (PD), is still debated. The older age and the multisystemic impairment of PD patients may render these patients a particularly vulnerable population, especially in advanced disease stages. Prevalence and outcome of COVID-19 in people with PD requires further clarification.

### **Recent developments**

Many studies reporting the impact of COVID-19 in PD patients have been published over the last few months. However, the relatively small sample size of PD patients with COVID-19 who were enrolled in most of them did not allow the authors to draw robust conclusions on whether the prevalence and outcome of COVID-19 in PD are different from those observed in the general population.

We conducted here a systematic review of published studies reporting data on PD patients with a diagnosis of COVID-19 (PD-COVID+). From each of them, we extracted prevalence, clinical-demographic data, outcome, and mortality of PD-COVID+. Comparisons between PD-COVID+ and control populations and specific inference or authors' notes on the presence of potential risk factors or protective factors were also analyzed.

We included 13 studies reporting on a total of 10,618 PD patients, 1,046 with a confirmed diagnosis of COVID-19. We found a median infection prevalence ranging from 0.6% to 8.5%. PD-COVID+ were males in 58.7% of cases, with a median age of 74 and disease duration of 9.9 years; 28.7% of the patients required hospitalization; 35.3% required an increase of the levodopa dose. The mortality rate was 18.8%.

Two case series and two cross-sectional studies suggested that 'advanced' PD stages might represent a risk factor for a worse COVID-19 outcome. Two case-control studies did not report significant differences in age and disease duration between PD patients with and without COVID-19. Amantadine and vitamin D were proposed as potential protective factors against Sars-Cov-2 infection.

### **Where next?**

Available studies indicate a higher risk of mortality in PD patients affected by COVID-19 compared to the general population. Conversely, available literature does not clarify whether PD patients are more susceptible to get infected. Cardiovascular risk factors and a long PD duration could be associated with a worse outcome; however, these aspects need to be replicated and further investigated in multicenter, case-control studies with adequate sample size. The potential protective role of vitamin D and, in particular, amantadine is intriguing, but deserves further investigations.

## INTRODUCTION

In late 2019, the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) began circulating across the world (biblio), and caused a human disease named coronavirus disease 2019 (COVID-19) (biblio). The most common symptoms of COVID-19 include fever, cough, and dyspnea, with the development of pneumonia or sepsis in a proportion of critical cases.<sup>1</sup> While the presence of neurological manifestations in patients with COVID-19 has been broadly reported,<sup>2</sup> the interaction between COVID-19 and pre-existing chronic neurological diseases still remains to be clarified. In particular, the impact of COVID-19 on people with Parkinson's disease (PD) is not well defined.<sup>3</sup> Pre-existing medical issues and older age have been associated with more severe manifestations of COVID-19 in the general population,<sup>4,5</sup> and neurological comorbidities seem to have an independent negative impact on SARS-CoV-2 infection's severity and outcome.<sup>6,7</sup> Moreover, the potential neurotropism of SARS-CoV-2,<sup>8,9</sup> the commonly observed presence of hyposmia in infected patients,<sup>10</sup> the potential expression of angiotensin-converting enzyme 2 (ACE2) in dopaminergic neurons and astrocytes mediated by inflammation,<sup>3,11</sup> and previous finding of antibodies against coronavirus in the cerebrospinal fluid of PD patients, prompted questions about the relationship between COVID-19 and PD.<sup>12</sup> Nonetheless, whether PD patients have a higher risk for developing COVID-19 or result in a significantly worse clinical outcome has not been elucidated yet.

We performed here a systematic review of the existing literature with the following aims: i) to summarize the prevalence, course, and clinical outcome of patients with PD who developed COVID-19 infection; ii) to identify the main clinical-demographic characteristics of infected patients; iii) to outline potential predictors of a worse clinical outcome alongside protective conditions.

## METHODS

We conducted a systematic review following the Preferred Reporting Items for Systematic Reviews and Meta-analyses (PRISMA).<sup>13</sup> PubMed was searched for case reports, case series, observational, cross-sectional, and case-control studies on October 21, 2020, reporting data on PD patients with a confirmed diagnosis of COVID-19 using the following search string: "Parkinson's disease AND COVID-19".

Abstracts and full-text articles were carefully reviewed to identify and exclude duplications of studies. Only studies referring to human subjects and published in English were considered. No restrictions were applied to sex, age, disease duration, disease severity, or follow-up. Each selected article's reference list was further reviewed to include any additional studies that were not captured by the original search strategy.

We used a standardized data collection form to extract, from each selected study, the following information where available: study design, criteria of patients' selection, country or region of the sample, number of enrolled patients, number of PD patients with a confirmed diagnosis of COVID-19 (PD-COVID+), sex, age, and disease duration of PD-COVID+, number of PD-COVID+ needing hospitalization, number of deaths among PD-COVID+, number of PD-COVID+ for whom dopaminergic therapy was augmented during COVID-19 infection, number of PD-COVID+ living in a nursing home. Moreover, when reported, data from the comparison between PD-COVID+ and control populations and specific inference or authors' notes about the presence of potential risk or protective factors were searched and registered.

Extracted data were analyzed and summarized by descriptive statistics, using prevalence, median, and range, or mean and standard deviation (SD).

## RESULTS

We included 13 studies (four case-control studies, three cross-sectional studies, five case series, and one case report)<sup>11,14-25</sup> (Figure 1, Table 1) reporting on a total of 10,618 PD patients, 1,046 with a confirmed diagnosis of COVID-19 (or, for two studies,<sup>14,15</sup> with either a real-time PCR assay or symptoms compatible with COVID-19 and ascertained contact with a PCR-confirmed case).

### **Prevalence of COVID-19 infection in patients with PD: clinical and demographic characteristics.**

The prevalence of COVID-19 infection among PD patients was available in six studies only.<sup>14,15,19,20,21,24</sup> It varied according to the geographical location, with a prevalence of 2.6% in Spain, 0.9% in the United States of America (USA), and variable values in different regions of Italy, ranging from 7.1-8.5% in Lombardy, 0.9% in Tuscany, and 0.6% in Piedmont.

PD-COVID+ were males in 58.7% of cases, with a median age of 74 years (range 65-80.5), and a median disease duration of 9.9 years (range 6.3-22). The mortality rate was 18.8% (n=197/1046). Data on hospitalization was reported in twelve studies, with a prevalence of 28.7% (n=101/352).<sup>11,14-21,23-25</sup> From five studies reporting such an information,<sup>11,14,18,20,25</sup> 35.3% of PD-COVID+ (n=12/34) required an increase of levodopa dose during the duration of infection, due to worsening of PD related symptoms. From four studies reporting the information,<sup>11,20,23,25</sup> 48.8% of PD-COVID+ (n=20/41) were living in a nursing home. It should be noted that this data was inflated by the extremely high percentage of PD-COVID+ (63.6%) reported in a single case-series on patients living in Connecticut, USA<sup>23</sup>. Excluding this study, the prevalence of PD-COVID+ from nursing homes is 30% (n=6/20).

From seven studies reporting the information,<sup>11,14,16,18,20,21,25</sup> 11.4% of PD-COVID+ (n=18/158) were treated with device-aided therapies: nine of them with levodopa/carbidopa intestinal gel infusion, eight with deep brain stimulation (two of them targeting the subthalamic nucleus, the remaining ones with an unknown target), and one with subthalamic deep brain stimulation and apomorphine pump.

### **Comparison with control groups**

Six studies reported comparisons between PD-COVID+ and PD patients who did not develop COVID-19 (PD-COVID-).<sup>14,15,19,21,22,24</sup> A study from Italian patients living in Lombardy compared 12 PD-COVID+ against 36 PD-COVID-, matched for sex, age, and disease duration. No between-group differences were found for body mass index, smoking habit, seasonal vaccination in 2019, PD phenotype, HY stage, diagnosis of dementia, and therapies, nor for comorbidities.<sup>14</sup> A study on Spanish patients reported that motor fluctuations, dementia, and behavioral disorders were present twice as much in PD-COVID- (n=553) compared to PD-COVID+ (n=15), with a trend towards a significant difference.<sup>19</sup> Moreover, cardiovascular risk factors and cardiovascular diseases were more frequently observed in PD-COVID+, with dyslipidemia being significantly more prevalent in this group.

Another study on Italian patients living in Lombardy, Italy, compared characteristics of PD-COVID+ vs. PD-COVID- and PD-COVID+ vs. family members without PD but affected by COVID-19.<sup>15</sup> The Authors found that PD-COVID+ (=105) individuals were younger, more frequently obese, and with a higher prevalence of chronic obstructive pulmonary disease than PD-COVID- (n=1,381). Moreover, a shorter hospitalization was needed for PD-COVID+ compared to family members with COVID-19 but without PD, while the mortality rate was similar between groups. A study on Italian PD patients living in Tuscany reported a higher prevalence of diabetes and hypertension in 7 PD-COVID+ when compared to 14 PD-COVID- matched for age and disease duration, in the absence of other differences in comorbidities or antiparkinsonian therapies.<sup>21</sup>

One study based on an electronic survey (with 80% of respondents living in the USA) found that PD-COVID+ (n=51) were more likely to be smokers and have a previous history of heart disease than PD-COVID- (n=5,378). Conversely, PD-COVID+ compared to people not suffering from PD who developed COVID-19 (n=26), were more likely to be older, male, and less likely to suffer from lung disease.<sup>24</sup>

Finally, one study specifically aimed at analyzing the case fatality of PD-COVID+ vs. people with COVID-19 and without PD: among 78,355 COVID-19 patients without PD, 4,290 died compared to 148 of the 694 PD-COVID+.<sup>22</sup> Moreover, the authors demonstrated that the mortality risk in people with PD is significantly higher than that of the general population (odds ratio 1.27), even when controlling for age, sex, and race differences.

### **PD duration**

Two case series<sup>11,16</sup> and one cross-sectional study<sup>20</sup> suggested that ‘advanced’ PD stages are a risk factor for a worse COVID-19 outcome. In particular, ten PD patients from Padua, Italy, and London, UK, were reported having an extremely high mortality rate (40%); given their mean age of 78.3 years and disease duration of 12.7 years, the authors hypothesized that older age and longer disease duration might increase patients’ susceptibility to severe COVID-19.<sup>11</sup> Similarly, a cross-sectional study reporting prevalence and outcome of COVID-19 in PD patients living in Piedmont, Italy, found a high mortality rate (75%) among eight PD-COVID+ with a mean age of 74 years and a disease duration of 12.1 years; in this study, patients’ mean age of death was 74.8 years, and the mean disease duration was 15 years.<sup>20</sup> Another case series of 117 PD-COVID+ individuals from tertiary centers in different countries identified a significant effect of concomitant dementia and PD duration on the mortality rate,<sup>16</sup> while a study based on an electronic survey reporting on 51 PD-COVID+ found that a longer PD duration is associated with a higher risk of pneumonia, the need for supplemental oxygen, or hospitalization.<sup>24</sup>

When considering the susceptibility for developing COVID-19, three case-control studies did not identify any significant differences in age and disease duration between PD patients with and without COVID-19.<sup>14,15,21</sup> Specifically, two studies observed that PD patients who developed symptomatic COVID-19 were neither older nor had a longer disease duration than those screening negative,<sup>14,21</sup> while the other one found a similar disease duration and an identical Hoehn and Yahr (HY) stage between PD-COVID+ and PD-COVID-.<sup>15</sup>

### **Protective factors**

Two studies highlighted some associations between the prevalence of COVID-19 and patient clinical features. In particular, one study on PD patients living in Lombardy, Italy, observed that a significantly higher percentage of PD patients who did not develop SARS-Cov2 infection were supplemented with vitamin D in comparison with those who developed infection (22.9% vs. 12.4%).<sup>15</sup> Another study on 568 Spanish PD patients who underwent an electronic interview reported that none of the 82 PD patients receiving amantadine was infected by COVID-19, with the difference showing a trend towards significance in comparison to patients who were not on amantadine therapy.<sup>19</sup> From eight studies reporting complete information on patients’ medication,<sup>11,14-16,19,20,23,25</sup> it appears that 2.4% of PD-COVID+ (n=7/290) were on amantadine treatment.

## **DISCUSSION**

In this review, we evaluated all published articles reporting data on PD patients with a confirmed diagnosis of COVID-19. The median prevalence of infection ranged from 0.6% to 8.5%, depending on the country and regions where patients lived. In most studies, the infection prevalence in the PD population was below 1%, while studies on patients living in Lombardy,<sup>14,15</sup> the first and most affected Italian region, showed the highest prevalence. From a total of 1,046 PD-COVID+, we found a hospitalization rate of 28.7% and a death rate of 18.8%. Noteworthy, from four studies reporting the information, we found that 48.8% of PD-COVID+ lived in a nursing home; however, excluding a single case-series on people living in Connecticut, USA, reporting a percentage of 63.6%,<sup>23</sup> the prevalence of PD-COVID+ living in a nursing home dropped to 30%.

On July 1<sup>st</sup>, 2020, the prevalence of COVID-19 in the general population of Italy, Spain, and the USA (the countries most represented in the included studies) was 0.4, 0.5, and 0.8%, respectively.<sup>26</sup> Thus, in most studies, the infection prevalence of PD patients was not consistently higher than the prevalence of the country's general population. On the contrary, a much higher COVID-19 prevalence in PD patients was found in the two studies reporting data from people living in Lombardy, Italy. Indeed, the prevalence of COVID-19 in Lombardy on July 1<sup>st</sup>, 2020 was 0.9%, significantly lower than the 7.1 and 8.5% found in PD patients of the same region.<sup>14,15</sup> The higher prevalence reported in Lombardy could be partially explained by the fact that the two studies also included patients without a molecular test confirmation, leading to a probable overestimation of the real COVID-19 prevalence in PD population. Moreover, the hypothesis that people with PD could be at higher risk of developing COVID-19 should take into account that PD patients have an older age than the general population, with age being a known risk factor for COVID-19.<sup>4,5</sup> On the other hand, the prevalence of infection could also be biased by more cautious PD patients' behavior since they have been considered a higher-risk population.<sup>14,19</sup> Thus, current literature does not help to definitely assert whether PD should be considered a risk factor for developing symptomatic COVID-19 infection.

We found more consistent evidence on the impact of COVID-19 in people with PD. Indeed, from a total of 1,046 PD-COVID+, 28.7% were hospitalized, and 18.8% died. These data point out towards higher frailty of PD patients. In fact, in October 2020, the death rates due to COVID-19 in Italy, Spain, and the USA were 2.7, 3.3, and 7.6%, respectively,<sup>26</sup> much lower than the percentage we obtained from the 13 studies included in our review. Likewise, one large sample study specifically aimed to analyze the case fatality of PD-COVID+ vs. people with COVID-19 and without PD demonstrated that the risk of death for COVID-19 in people with PD was about 30% higher than the general population, after adjusting the statistical analysis for age, sex, and race differences.<sup>22</sup>

Summarizing data from all studies, we found a slightly higher prevalence of males (58.7%), probably reflecting the higher number of males affected by PD,<sup>27</sup> a median age of infected patients of 74 (range 65-80.5), and a median disease



duration of 9.9 (range 6.3-22). These findings seem to imply a higher susceptibility to COVID-19 for PD patients with older age and longer disease duration, as suggested by some studies,<sup>11,15,20</sup> although available case-control studies did not confirm this hypothesis.<sup>14,15</sup> Studies with control groups found no consistent correlations between specific clinical features and the risk of being infected. In fact, one study with sex-, age-, and disease duration-matched control group did not find significant differences for body mass index, smoking, seasonal vaccination in 2019, PD phenotype and stage, therapies, and comorbidities,<sup>14</sup> while the study on Spanish PD patients found a trend toward a higher severity of motor fluctuations and neuropsychological issues in patients without COVID-19 infection.<sup>19</sup> Remarkably, one study found that infected PD patients were significantly younger and more frequently obese than PD patients without a diagnosis of COVID-19.<sup>15</sup> Cardiovascular risk factors and a higher prevalence of chronic obstructive pulmonary disease were found as predisposing factors for getting COVID-19 infection among PD patients, as for the general population.<sup>5,15,19,24,28</sup>

Some potential protective factors have been proposed. The study on 568 PD patients living in Spain found that none of the 82 patients receiving amantadine was infected by SARS-CoV-2.<sup>19</sup> Another study on 15 patients with neurological diseases (PD or multiple sclerosis) who were taking amantadine reported no signs or symptoms of infection despite a confirmed diagnosis of COVID-19.<sup>29</sup> Our review evidenced that among a total 290 PD patients with COVID-19 for whom therapy information was available, only seven (2.4%) were treated with amantadine. The potential of amantadine as a protective drug is further supported by a drug screen gene expression study suggesting that amantadine could decrease the replication and infectivity of the SARS-CoV-2.<sup>30</sup> Altogether, these data make amantadine a promising drug to protect from COVID-19 viral replication *in vivo*.

The second potential protective factor suggested by published studies and supported by its biological characteristics is vitamin D. It has been hypothesized that vitamin D could reduce the risk of infection through several mechanisms, such as by reducing concentrations of pro-inflammatory cytokines.<sup>31</sup> Moreover, two studies investigating the effect of vitamin D levels in the general population found an inverse association between serum concentration and both prevalence and mortality of COVID-19,<sup>28,29</sup> although this evidence requests confirmations in randomized control trials and further cohort studies.<sup>30</sup> Even in the limited number of literature data on COVID-19 in PD, a correlation between higher vitamin D intake and lower risk of COVID-19 was found.<sup>15</sup>

In conclusion, available literature points out a possible worse COVID-19 outcome in people with PD. On the contrary, data published so far do not provide sufficient evidence for considering PD patients at a higher risk of COVID-19 infection. Pending further studies, a longer PD duration could be regarded as a potential risk factor for higher susceptibility and worse outcomes in PD patients with COVID-19, as well as older age and cardiovascular or pulmonary comorbidities. Finally, the role of vitamin D and amantadine in making PD patients less prone to develop

the infection or severe symptoms seems particularly intriguing and need confirmation by specific studies to clarify their protective action.

In this review, we evaluated all published articles reporting data on PD patients with a confirmed diagnosis of COVID-19. The median prevalence of infection ranged from 0.6% to 8.5%, depending on the country and regions where the patients lived. In most studies, SARS-CoV2 infection prevalence in the PD population was below 1%, with the exception of studies on patients living in Lombardy,<sup>14,15</sup> the first and most affected Italian region by COVID-19 pandemic, which showed the highest prevalence. From a total of 1,046 PD-COVID+ patients, there was a hospitalization rate of 28.7% with a mortality rate of 18.8%. Noteworthy, from four studies reporting such an information, 48.8% of PD-COVID+ patients were living in a nursing home. If we exclude the single case-series from people living in Connecticut, USA, reporting a percentage of 63.6%,<sup>23</sup> the prevalence of PD-COVID+ living in a nursing home drops to 30%.

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We found more consistent evidence on the clinical impact of COVID-19 in people with PD. Indeed, from a total of 1,046 PD-COVID+, 28.7% were hospitalized, and 18.8% died. These data point out towards a higher frailty of PD patients. In fact, in October 2020, the mortality rates due to COVID-19 in Italy, Spain, and the USA were 2.7, 3.3, and 7.6%, respectively,<sup>26</sup> which is much lower than the percentage we derived from the 13 studies included in the current

review. Likewise, one large sample study that specifically aimed at analyzing the case fatality of PD-COVID+ vs. people with COVID-19 and without PD, demonstrated that the risk of death for COVID-19 in people with PD is about 30% higher than in the general population, after adjusting the statistical analysis for age, sex, and race differences.<sup>22</sup> Summarizing data from all studies, we found a slightly higher prevalence of males (58.7%), probably reflecting the higher number of males affected by PD,<sup>27</sup> a median age of infected patients of 74 yrs (range 65-80.5), and a median disease duration of 9.9 yrs (range 6.3-22). These findings indicate a higher susceptibility to COVID-19 for PD patients with older age and longer disease duration. This is suggested by some studies,<sup>11,15,20</sup> although available case-control studies did not confirm such an hypothesis.<sup>14,15</sup> Studies that included control groups found no consistent correlations between specific clinical features and the risk of being infected by Sars-CoV-2. In fact, one study including a sex-, age-, and disease duration-matched control group did not report any significant differences in body mass index, smoking, seasonal vaccination in 2019, PD phenotype and stage, therapies, and comorbidities.<sup>14</sup> Conversely, a study on Spanish patients with PD reported a trend toward a higher severity of motor fluctuations and neuropsychological impairments in those patients who did not develop COVID-19 infection.<sup>19</sup> Remarkably, one study found that PD-COVID+ were significantly younger and more frequently obese than PD-COVID-.<sup>15</sup> Cardiovascular risk factors and a higher prevalence of chronic obstructive pulmonary disease were found as predisposing factors for developing COVID-19 infection among PD patients, as for the general population.<sup>5,15,19,24,28</sup>

Some potential protective factors have been proposed. The study on 568 PD patients living in Spain found that none of the 82 patients receiving amantadine resulted being infected by SARS-CoV-2.<sup>19</sup> Another study on 15 patients with neurological diseases (PD or multiple sclerosis) who were on amantadine therapy reported no signs or symptoms of infection despite a confirmed diagnosis of COVID-19.<sup>29</sup> Our review highlighted that among a total number of 290 PD patients with COVID-19 for whom therapy information was available, only seven (2.4%) were on amantadine therapy. The potential of amantadine as a protective drug is further supported by a drug screen gene expression study suggesting that amantadine could decrease the replication and infectivity of the SARS-CoV-2.<sup>30</sup> Taken altogether, these data make amantadine a promising drug to protect from COVID-19 viral replication *in vivo*.

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In conclusion, available literature points out a possible worse clinical outcome in people with PD who develop COVID-19. On the contrary, data published so far do not provide sufficient evidence for considering PD as a condition at higher risk for COVID-19 infection. Pending further studies, a longer PD duration could be regarded as a potential risk factor for higher susceptibility and worse outcomes in PD patients with COVID-19, as well as older age and cardiovascular or pulmonary comorbidities. Finally, the role of vitamin D and amantadine in making PD patients less prone to develop COVID-19 infection or severe symptoms is particularly intriguing but needs confirmation by tailored clinical trials to clarify their protective action.

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**Table 1. Included studies**

	Geographical area	Study design	Selection	PD-COVID+	Sex (males)	Age	Disease duration	Hospitalization	Comorbidities	Death	Nursing home	Levodopa increase	Device-aided therapy
Antonini et al. 2020	Italy/UK (Padua-London)	Case series	NA	2 advanced PD from Italy + 8 advanced PD from UK	6 (60%)	78.3	12.7	3 required CPAP or ICU	10	4 (40%)	2	5	3 LCIG, 1 STN-DBS + apomorphine pump
Cilia et al. 2020	Italy (Lombardy)	Case control	Random selection of 141 PD for interview	12	5 (41.7%)	65.5	6.3	1	9	0 (0%)	NR	4	1 LCIG
Fasano et al. 2020	Italy (Lombardy)	Case control	1486 PD patients living in Lombardy and with at least one visit at the tertiary center Parkinson institute of Milan	32 PD COVID+ confirmed + 73 PD COVID+ probable	55 (52.4%)	70.5	9.9	18	78	6 (5.7%)	NR	NR	NR
Fasano et al. 2020	Italy, Iran, Spain, UK	Case series	NA	117	74 (63.2%)	71.4	9.4	37	97	23 (19.7%)	NR		4 LCIG, 6 DBS
Filatov et al. 2020	China	Case report	NA	1	1 (100%)	74	NR	1	1	“Critical ill”	no	NR	NR
Hainque et al. 2020	France	Case series	NA	2	1 (50%)	78	22	2	NR	2 (100%)	no	1	2 STN-DBS
Santos Garcia et al. 2020	Spain	Cross-sectional	568 PD patients or caregivers reached by interview on voluntary basis	15	7 (46.7%)	65.6	6.8	5 (1 in ICU)	NA	0 (0%)	NR	NR	NR
Artusi et al. 2020	Italy (Piedmont)	Cross-sectional	1407 random PD patients living in Piedmont	8	5 (62.5%)	74	12.1	7	6	6 (75%)	3	1	1 LCIG
Del Prete et al. 2020	Italy (Tuscany)	Case control	740 non-demented PD patients who had performed at least one outpatient visit from	7	4 (57.1%)	75.7	9.3	4	NR	1 (14.3%)	NR	NR	0

			January 1th to December 31th 2019 living in Tuscany										
Zhang et al. 2020	Mostly USA	Case control	All COVID+ patients via the TriNetX COVID-19 research network	694	418 (60.2%)	79	NR	NR	NR	148 (21.3%)	NR	NR	NR
De Marcaida et al. 2020	USA (Connecticut)	Case series	All COVID-19 positive patients with movement disorders from the Chase Family Movement Disorders Center (CFMDC) and PD-COVID+ admitted to affiliate hospitals in Connecticut	21	13 (59.1%)	75.2	9.9	16	18	6 (28.6%)	14	NR	NR
Brown et al. 2020	Mostly USA	Cross-sectional	All people with and without PD participating in the online study Fox Insight who responded to online survey	51	24 (47%)	65	NA	5 (2 in ICU)	NA	0 (0%)	NR	NR	NR
Lo Monaco et al. 2020	Italy (Rome)	Case series	Description of five patients with parkinsonism, who tested COVID-19 positive at the Fondazione Policlinico Universitario “Agostino Gemelli”	2	1 (50%)	80.5	NR	2	2	1 (50%)	1	0	0

PD: Parkinson's disease

COVID+: patients with Parkinson's disease with a diagnosis of COVID-19

LCIG: Levodopa/Carbidopa intestinal gel infusion

DBS: deep brain stimulation

STN: subthalamic nucleus

NA: not applicable

NR: not reported

ICU: intensive care unit

**Figure 1. Flow-chart of the systematic review**